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09/998,832	11/29/2001	Robert Chow	020035-001100US	7166

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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,832	CHOW ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15-18,20,24,25 and 27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,15-18,20,24,25 and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/21/02; 11/29/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment filed July 17, 2006 has been received and entered. Claims 2-14, 19, 21-23, 26 have been cancelled, while applicants have added new claims 32-34.

Newly added claims 32-34 are generally drawn to a method for preventing or treating HIV infection caused by macrophage tropic strain of HIV in human by transplanting stem cell rich population of cells having beneficial gene that is polymorphism in a CCR5 gene.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application was eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action was withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/9/2005 was entered.

Claims 1, 15-18, 20, 24-25, 27-31 and newly added claim 32-34 are under consideration.

Declaration

The declaration filed on July 17, 2006 under 37 CFR 1.132 is sufficient in part to overcome the rejection of claims 1, 15-18, 20, 24-25 and 27-34 upon declaration of Drs. Chow and Petz, applied under 35 U.S.C. 112 First paragraph. The declaration will be discussed in detail below as it applies to the rejection.

Maintained-Double Patenting

Claims 1, 15-18, 20, 24-25 and 27-31 and newly added claims 32-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting

as being unpatentable over claims 1-35 of copending Application No. 10/498450 (US Patent Publication no 20050220772). Even though the conflicting claims are not the same, they are not patentably distinct from each other because both sets of claims encompass a method of treating or preventing HIV infection by transplanting stem cells having a beneficial gene. For example, claim 1 of instant application encompasses a method for preventing or treating HIV infection caused by M-tropic virus in humans by transplanting stem cell rich population of cell that has beneficial gene that is polymorphism in CCR5 gene. Claims 15-17 depend on method of claim 1 wherein polymorphism is either a 32-basepair deletions in coding region or CCR5m303 or in promoter region. Claim 18 depends on method of claim 1 wherein stem cell population will be selected from bone marrow, peripheral blood, umbilical cord blood and adipose tissue. Remaining claims are directed to screen cell sample from human donor to identify stem cell population having beneficial gene and identification of HLA genotype or phenotype. Whereas, Claim 1 of the application No. 10/498450 is directed to a method of treating or preventing HIV infection in humans by screening plurality of cells to identify stem cells having beneficial gene and then transplanting stem cell with beneficial gene into HIV infected patients. The remaining claims 2-33 encompass all the limitations of instant application. Thus, the claims of application no 10/498450 (US Patent publication no 20050220772) differ only with respect to broader scope of beneficial genes that could be used in the method for treating or preventing HIV infection, which encompasses polymorphism in CCR5 specifically claimed in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

New-Claim Rejections-Necessitated by Amendments - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 15-18, 20, 24-25 and 27-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

37 CFR 1.118(a) states "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". In the instant case, the recitation of limitation... "caused by a macrophage tropic strain of HIV in a human.." (claims 1 and 32) is considered new matter.

Applicants point to page 1, lines 17-28 of the specification for the specific support of the claimed amendment reciting the a method for preventing or treating HIV infection caused by a macrophage tropic strain of HIV. However, upon further review of the instant specification, Examiner could only find support for a general description of chemokine receptors CCR5 that binds to RANTES, MIP-1 alpha, and MIP-1 beta, and

serves as a co receptor for macrophage tropic- strains of HIV. Contrary to the support fro M-tropic virus strain, the specification at several instances made reference to the methods of this invention could be used to treat or prevent any disease or condition that arises from HIV infection, such as AIDS and ARC (see page 4, page 12, lines 22-23, page 13, lines 10-11 and abstract).

Furthermore, specification provides no link to show that the treatment directed to individual suffering from any disease associated with any specific strain of HIV in human. It is emphasized that the specification only provides support directly to existence of different receptors on HIV and not to any method of treating or preventing HIV infection caused by any specific strain of HIV. In fact, through out the specification and in abstract Applicants only contemplated treating or preventing not only HIV infection but also any disease associated with HIV which embraces all different strains and variants of HIV.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981) teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time application was filed...If a claim is amended to include subject matter, limitation or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes, "When an amendment is filed in reply to an objection or rejection based on U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendment made to the disclosure".

To the extent the claimed method is not described in the instant disclosure, claims 1, 15-18, 20, 24-25 and 27-34 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention, since the applicants disclosure do not teach a method that is adequately described in the specification. In this case, it appears that the claims reflect a method of treating or preventing HIV infection caused by a macrophage tropic strain of HIV. The claims as amended only have one functional characteristics that is HIV is prevented or treated that is caused by M-tropic virus using the method disclosed in the specification. A review of art suggest that HIV-1 tropism for macrophages and microglia is restricted at the entry level by a mechanism independent of co receptor specificity (Gorry et al Journal of Virology 2001 Nov;75(21):10073-89). Gorry et al using TAK-779 and AMD3100 show that two highly M-tropic isolates entered microglia primarily via CXCR4. These findings provide evidence that entry of even M-tropic virus is independent of co receptor and simply providing, cell that have polymorphism in CCR5 would not have resulted in the treatment or prevention of HIV and would constitute an enormous amount of experimentation to empirically test presence of other co receptor usage in M-tropic infection to determine if M-tropic virus would use only CCR5 co receptor. As described before, the specification does not provide adequate guidance on determining what is included or excluded by the claims as amended and therefore an artisan of skill would require undue experimentation to practice or make and/or use the invention.

New-Claim Rejections-Necessitated by Amendments- 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 15-18, 20, 24-25 and 27-31 remain rejected under 35 U.S.C. 112, and newly added claims 31-34 are also rejected first paragraph under 35 U.S.C. 112, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 encompasses a method of preventing or treating HIV infection in a human by transplanting a stem cell rich population of cells obtained from a human donor having beneficial gene that is a polymorphism in a CCR5 gene. Claims 15-17 depend on method claim 1 wherein polymorphism is either a 32-basepair deletions in coding region or CCR5m303 or in promoter region. Claim 18 depend on method of claim 1 wherein steam cell population will be selected from bone marrow, peripheral blood, umbilical cord blood and adipose tissue. Claim 20 describes the method of transplanting a stem cell rich population further comprises identification of the HLA genotype or phenotype of stem cell rich population. Claims 24-25 encompass method of screening cell sample from human donor to identify the stem cell rich population of the cell that has polymorphism in CCR5 gene by different techniques. Claims 27-31 encompass stem cell rich population of cells are from umbilical cord blood subsequent claims disclose a method-comprising identification of HLA genotype via high throughput such that genotype or phenotype of such cell is compatible with HLA genotype or phenotype of human.

The application as filed is not enabling for the invention because art of preventing or treating HIV by transplanting a stem cell rich population of cells obtained from a human donor having any beneficial gene was unpredictable as has been recognized by the art of skill and therefore require undue experimentation. As will be shown below, these aspects as well as limitations were not enabled for the claimed invention at the time of filling of this application because neither the specification nor the art of record taught sufficient guidance to practice the claimed invention.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ 1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the

invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled commensurate with the full scope of the claims.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working example are not disclosed in the specification, therefore enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore, skepticism raised in enablement rejections are those raised in the art by artisan of expertise.

Claims 1, 15-18, 20, 24-25 and 27-34 are broad in scope. The following paragraph will outline the full scope of the claims:

Claimed invention recites a method of preventing or treating HIV infection caused by M-tropic strain of HIV in human by transplanting a stem cell rich population of cells having a beneficial gene that is a polymorphism in a CCR5 gene. Since these claims encompass treatment or prevention of HIV infection caused by M-tropic strain of HIV by transplanting any umbilical cord blood stem cell rich population, any mutation in any part of the gene subsequently limiting to either promoter or coding region of CCR5. The disclosure provided by the applicant, in view of prior art, must encompass a wide area of knowledge to a reasonably comprehensive extent. In other word each of these, aspect must be shown to a reasonable extent so that one of the ordinary skills in the art would be able to practice the invention without any undue burden being on such Artisan.

The specification as filed provides a general description of polymorphisms of genes encoding ligand for the co receptor CCR5 and CXCR4 that confer resistance to HIV (pp 1). The specification also states that HLA alleles influence HIV-1 disease progression (refer pp 1-2). Remaining specification discloses definition of terms, general description of biological method, method of stem cell transplant and HLA genotyping.

Furthermore, it is noted that application as filed itself states "the discovery of the fact that certain polymorphism confer resistance to HIV has led to proposal of therapies which repopulate the immune system with cells that could confer resistance to HIV infection". The specification also states, "nature of such therapies should reduce side effect" suggesting that treatment or prevention against HIV infection by transplanting stem or any other cell to confer resistance to HIV infection was just a theory that was not reduced to practice at the time of filing of this application as neither art nor specification specifically teaches how stem cell having beneficial gene that is polymorphism in a CCR5 gene would have prevented or treated HIV infection. In summary, the specification does not provide any specific guidance for the claimed invention because the specification as filed does not teach how to many stem cells would be enough to confer resistance in a subject already infected with any strain of HIV as compare to a normal healthy individual for prevention of HIV infection.

The method of treating or preventing HIV infection by transplanting stem cell derived from human was not routine, rather was unpredictable at the time of filing of this application as neither art of record nor the specification teaches how to practice the claimed inventions. Given this lack of reasonable predictability in specification and the art, the Artisan would require a large amount of information from Applicant's examples to provide the guidance to provide reasonable predictability.

Applicant example only provides a schematic of proposed therapy in human without disclosing any specific. In addition, Applicants do not provide any disclosure on how stem cell deficient in CCR5 delta 32 will be grown *ex vivo* or *in vivo*. Furthermore, it is not enough to reasonably predict that the stem cell rich population with CCR5 polymorphism administrated at reasonable level for appropriate time duration in human would be efficacious in treating or preventing HIV infection. The specification fails to provide an enabling disclosure for the claimed invention because the specification fails to provide sufficient guidance as to how an artisan of skill would have practiced the claimed method for treating or preventing HIV infection caused by a macrophage tropic strain of HIV in a human. An artisan would have to carry out extensive experimentation to make use the invention, and such experimentation would have been undue because

of the art of stem cell transplant in HIV infection caused by any specific strain of virus was not routine rather it was unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.
As a first issue, claims 1, 15-18, 20 and 27-34 require stem cell rich population of cells from any human donor having beneficial gene that is polymorphism in a CCR5 gene. However, art of record shows that beneficial gene is not present uniformaly in human population. For example, Lucotte (Hum Immunol. 2001: 62(9):933-6; and references therein) discloses the allelic frequency of 32 basepair deletion is very rarely seen in African population and only 10% population of European desent are homozygous for 32 basepair deletion, which only partially protects against HIV infection (pp 933, right column, lines 1-6). It is also not apparent how skilled artisan without any undue experimentation, practices method as contemplated by the instant claims particularly given the unpredictability of growing stem cell deficient in CCR5 delta 32 *ex vivo* or *in vitro* and unpredictability expressed in the art and discussed in this and previous office actions.

As a second issue, instant claims read on treating or preventing HIV infection cause by a macrophage tropic strain of HIV in a human by transplanting into human a stem cell rich population of cell that has beneficial gene that is a polymorphism in a CCR5 gene. However, Naif et al (Journal of Virology, 2002, 72(1): 3114-3124) demonstrates the ability of certain strains of HIV to readily use CXCR4 for infection or entry into macrophages, which is highly relevant to the pathogenesis of late-stage disease and presumably HIV transmission (abstract). Naif et al show that a primary HIV isolate from an HIV-infected CCR5-deficient person can infect both macrophages and T-cell lines via the co receptor CXCR4. This is further supported by the studies of Gorry et al showing HIV-1 tropism for macrophages and microglia can be restricted at the entry level by a mechanism independent of co receptor specificity (Gorry et al Journal of Virology 2001; 75(21): 10073-89). It is noted that Gorry et al use CCR5 and CXCR4 inhibitorsTAK-779 and AMD3100 to show that two highly M-tropic isolates entered microglia primarily via CXCR4. This clearly supports the fact that HIV-1 tropism for macrophage and microglia is independent of any specific receptor. Further, Gorry et al

state "M-tropic HIV-1 viruses typically utilize CCR5 for entry in primary $CD4^+$ cells. However, our studies showed that CCR5 usage is neither necessary nor sufficient for M-tropism. We found that 6 of 11 primary R5 isolates could not replicate in monocyte-derived macrophages (MDM) and microglia. Furthermore, inhibition of CXCR4 by 12G5 or AMD3100 abolished virus replication in microglia by the highly M-tropic R5X4 isolates, indicating that these isolates entered cells primarily via CXCR4. These findings are consistent with previous studies that failed to establish a strict correlation between CCR5 usage and M-tropism and showed a lack of M- tropism by some R5 HIV-1 clones obtained from brain, lymph node, spleen, and lung tissue". Furthermore, Sheppard et al (Journal of acquired Immune Deficiency Syndrome, 29: 307-313) disclose that delta 32 mediated resistances to HIV are incomplete and are associated with acquisition of exclusively-X4 variants of HIV-1 (abstract, pp311). In addition, it is emphasized that Sheppard et al state " further studies are needed to explore the relationship between pattern of co receptor usage and mechanism of pathogenesis (pp312, column 2, paragraph 2). This in conjunction with Dean and O'Brien (1997) as discussed in previous non final and Final office action (dated 11/2/2004) clearly establishes the unpredictability of treating preventing or treating HIV infection caused by any specific strain by transplanting stem cell having beneficial gene that has polymorphism in CCR5 gene. The specification does not provide sufficient guidance to overcome this unpredictability for practicing the claimed method in-patient infected with M-tropic strain of HIV. The specification does not provide any guidance as to how would an artisan select which polymorphism that will be beneficial for preventing or treating HIV infection caused by M-tropic strain of virus. Therefore, at the time of the invention there was no evidence of treating or preventing HIV infection caused by M-tropic virus strain in humans by transplanting stem cells with any beneficial gene having polymorphism and treatment or prevention of a HIV infection would have been unpredictable since a number of factors played role in the process of blocking infection as evident from the art of record.

As a third issue, specification also does not provide disclosure on number of stem cell that are required to be transplanted to elicit specific protective response. It is

also not apparent how stem cell with beneficial gene having polymorphism could prevent HIV infection caused by M-tropic strain of virus, since art has already indicated that two highly M-tropic isolates entered microglia primarily via CXCR4 (supra) . It is noted that Dr. Chow declaration describe number of cells would be dependent on the body weight of the patient. It is emphasized that as discussed in the specification, the art reported correlation of HIV co-receptor CCR5 polymorphism in HIV infected patients with disease progression (see McDermott et al. The Lancet 352:866-870, 1998 ; references of the record), however, the art of record did not teach how to treat or prevent HIV infection in a patient by transplanting stem cells that have the protective polymorphism. However, as stated before in this office action, art of record teaches that HIV infection could use many alternate receptor and without any specific guidance, an artisan would have to perform undue experimentation to expand enough of umbilical cord blood derived stem cell comprising CCR5 gene to test whether it would confer resistance to HIV infection cause by M-tropic strain of HIV, which would be dependent on numerous factors including receptor usage and severity of infection.

In conclusion, in view of breadth of the claims and absence of a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled for the claimed inventions. The specification and prior arts do not teach a method of treating or preventing HIV infection in human by transplanting stem cell population having a beneficial gene that is polymorphism in CCR5 gene in humans. An artisan of skill would have required undue experimentation to practice the invention because the art of ex *vivo* cell therapy for the treatment or prevention of HIV in general was unpredictable at the time of filing of this application as supported by the observations in the art record.

Response to Arguments

Applicant arguments filed on July 17, 2006 have been fully considered but they are not fully persuasive.

Applicant in their argument on page 6, argue that Examiners improperly focused on inoperative embodiments and these embodiments are fully enabled. However, these arguments are not fully persuasive because the enablement rejection was not based on the inoperative embodiments rather on what has been taught in the specification for practicing the claimed invention and what is known in the art and whether an artisan of skill could make and use the claimed invention without undue experimentation. In response to applicants' discussion of *In re Cook and Merigold 169 USPQ 302* and *Ex Parte Forman 230 USPQ 546*, it is noted that these case laws are not applicable in this case because, first, no embodiment is enabled in the instantly claimed invention and second, the enablement rejection was based on analysis according to In re Wands, as discussed in the MPEP. In contrast to applicants' arguments, Courts have stated, eg., "It is true, as Genentech argues, that a specification need not disclose what is well known in the art. See, e.g., *Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986)*. However, that general, off-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." (See *Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)*).

On pages 7 and 8, Applicants argue that they satisfy the enablement requirement as dosage of stem cell and transplantation of hematopoietic stem cell derived from cord blood to person with HIV infection was routinely practiced at the time of filing and did not require undue experimentation. Applicants provide declaration of Drs. Chow and Petz showing the use of umbilical cord blood at the time of filing of this application. The declaration by Drs. Chow and Petz is persuasive in part; hence, rejections pertaining to

expansion of cord blood cell consistent with the declaration are withdrawn. However, declaration of dosage of stem cell for the treatment or prevention is not fully persuasive because number of stem cell will be solely dependent on severity of infection and usage of alternate co receptor as discussed in this office action.

On page 9, Applicants argue that example 1 and 2 provide disclosure of screening multiple cord blood samples to identify a source of stem cell that has a potential gene. Applicants assert that sources of stem cells with beneficial gene could be identified and could be collected for the use. In response, it is emphasized that independent claims 1 and 32 require transplanting into human a stem cell rich population of cells from a human donor that has beneficial gene. It is noted that art of record suggest that beneficial gene that has a polymorphism in CCR5 gene is not uniformly present in population (supra). Since independent claims 1and 32 do not recite any screening step for CCR5 polymorphism, it is not clear how stem cell from any human donor could be transplanted which will have this beneficial gene.

On page 10, Applicants argue that Roman et al do not contradict that in certain circumstances a CCR5 polymorphism did not provide resistance to HIV infection. In response, Applicants arguments are persuasive since Roman et al show overall allele frequencies are comparable to frequencies reported in previous studies in Caucasian populations. Therefore, rejection pertaining the reference of Roman et al is withdrawn.

Lastly, Applicants argue that CCR5 beneficial mutations were identified in person infected with HIV for long period before onset of AIDS or who appeared to not develop AIDS. Applicants argue that any delay in AIDS onset is efficacious and provides a treatment for HIV infected patient.

In response, it is emphasized that Applicants argument that CCR5 mutation in subject with infected HIV shows delay in progression of disease is not persuasive in a transplant method as recited in this application. In the instant case, the real issue is whether transplant of stem cell that has beneficial gene would confer any resistance to a subject to either prevent or treat HIV infection caused by M-tropic strain of virus. It is clear from the cited art, that M-tropic HIV-1 viruses that typically utilize CCR5 for entry in

primary $CD4^+$ cells may not require CCR5 in late stage of infection. A general review of the art also suggest that M-tropic strain that readily uses CXCR4 for infection or entry into macrophages, during the pathogenesis of late-stage disease (supra), therefore it is not clear whether a subject with late stage disease would have any effect with transplant method as contemplated in this application.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272- 0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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